REMARKS

Claims 19-36 are pending. Claim 19 has been amended. Claims 23-36 are new. The disclosure provides adequate written description for claims drawn to kits comprising instructions for the use of an anti-CD2 antibody an immunosuppressive agent. See, for example, page 61, lines 6-8 of the specification, where it states

> An anti-CD2 antibody, preferably a monoclonal, e.g., BTI-322, or a monoclonal directed at a similar or overlapping epitope, can be used in addition to or in place of any anti-T cell antibodies (e.g., ATG) in any method referred to herein. (emphasis added)

At page 4, lines 16-18, in preferred embodiments, the method can include, "prior to hematopoietic stem cell transplantation, introducing into the recipient an antibody capable of binding to mature T cells of said recipient mammal."

Other such methods in which anti-T cell antibodies can be used, are described throughout the specification. See, for example, the method described at page 4, lines 21-29, and preferred embodiments of the method at page 7, lines 33-35. See also the method described at page 9, lines 32-38, and preferred embodiments at page 10, lines 21-25. Additional methods are disclosed in the specification.

Support for administering a short course of a high dose of an immunosuppressive agent, as provided by instructions in the claims, can be found throughout the specification. See, for example, page 1, lines 17-21, which states

> The invention provides several methods of inducing tolerance to foreign antigens, e.g., to antigens on allogeneic or xenogeneic tissue or organ grafts. These methods can be used individually or in combination with one another. For example, it has been found that the short-term administration of a help-reducing agent, e.g., a short high dose course of cyclosporine A (CsA), can significantly prolong graft acceptance.

Support can also be found at page 18, lines 17-25, and page 50, lines 17-18 of the specification. Support for administering a short course of the immunosuppressive agent can be found throughout the specification. See, for example, the passage above (page 3, lines 1-11).

Support for new claim 25 can be found, e.g., at page 18, lines 17-23. Support for new claim 26 can be found, e.g., at page 22, lines 8-9. Support for new claims 27 and 28 can be found, e.g., at page 18, lines 22-23. Support for new claims 29, 30, and 31 can be found, e.g., at page 2, lines 16-22. Support for new claim 32 can be found at, e.g., page 3, lines 29-31. Support for new claims 33 and 34 can be found at, e.g., page 1, lines 33-35. Support for new claims 35 and 36 can be found, e.g., at page 61, lines 6-8. No new matter has been added by this amendment.

Priority

The Examiner statement that the effective filing date for claims 19-23 is the filing date of U.S.S.N. 08/458,720, June 1, 1995, is acknowledged.

Rejections Under 35 U.S.C. § 102

Claims 19-20, and 23 are rejected under 35 U.S.C. § 102(b) as anticipated by Chavin et al. ("Chavin"). The Examiner states

> Since the word 'kit' has not been defined in the specification, the claims have been interpreted according to applicant's description of a combination of an anti-CD2 antibody and an immunosuppressive agent. Chavin et al. teaches the combined administration of a monoclonal anti-CD2 antibody and an immunosuppressant such as cyclosporine, rapamycin or FK506 in order to increase graft survival in murine cardiac allograft recipients...Thus by teaching all the elements of the claims as written, Chavin et al. clearly anticipates the instant invention.

This rejection is respectfully traversed. As amended, the claims are directed to kits comprising: an anti-CD2 antibody or an antigen-binding fragment in a pharmaceutically acceptable carrier, an immunosuppressive agent, and instructions to administer a short course of the immunosuppressive agent at a high dose.

Chavin et al. does not disclose all of the elements of the present claims. Chavin et al. does not implement or describe a short course of administration of a high dose of an immunosuppressive agent. Rather, Chavin et al. teaches administration of immunosuppressive agents for at least 14, 21, and 60 days after donor graft implantation, and is silent with respect to selection of a time course for administration, other than to note that the longest time course, 60 days, worked the best in their method. See page 738, paragraph 1 of the Discussion section, where Chavin et al. states "the results reported here show that a 60-day course of subtherapeutic FK506 synergizes with anti-CD2 mAb and induced donor-specific tolerance." In addition, Chavin et al. disclose using low dose administration of the immunosuppressive agent, and suggest that such "subtherapeutic" doses are preferable. See, for example, the first paragraph after the abstract on page 736, where it states

> The use of [cyclosporine, FK506, and rapamycin] has fallen short of the ultimate goal of transplantation, i.e., the induction of tolerance. In addition, each of these immunosuppressants has associated toxicities when used at therapeutic doses.

Chavin et al. is concerned with administration of low, subtherapeutic doses of immunosuppressive agents and does not provide information for high dose, short course administration of the immunosuppressive agent as recited in the claims. Thus, Chavin et al. does not disclose each and every element of the claims, and therefore does not anticipate the claimed invention.

Rejections Under 35 U.S.C. § 103

Claims 21 and 22 are rejected under 35 U.S.C. § 103(a) as unpatentable over WO 94/20619 (Bazin et al.) in view of Chavin et al. The Examiner states

> Based on the motivation provided by Chavin et al. for combining the anti-CD2 antibody and FK506 to inhibit graft rejection, it would have been prima facie obvious to the skilled artisan to administer FK506 with the LO-CD2a antibody as taught by Bazin et al. in order to effect a synergistic increase in tolerance induction in humans with a reasonable expectation of success.

This rejection is traversed with respect to the presently pending claims. Claims 21 and 22 depend from claim 19. Claim 19, as amended, is directed to a kit that comprises an anti-CD2 antibody or an antigen-binding fragment thereof in a pharmaceutically acceptable carrier, an immunosuppressive agent, and instructions to administer a short course of the immunosuppressive agent at a high dose. As discussed above, Chavin et al. does not teach administration of a short course of an immunosuppressive agent in a high dose. Bazin et al. also does not teach or suggest administration of a short course of an immunosuppressive agent in a high dose. Therefore, Bazin et al. do not make up for the deficiencies of Chavin et al. Thus, the teachings of Chavin et al. and Bazin et al., either alone or in combination, fail to teach or suggest the claimed invention.

Applicant asks that the rejection of the claims be withdrawn.

Enclosed is a $110 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 7/25/03

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